

Listing of Claims

1. (original) An isolated variant platelet derived growth factor receptor alpha (PDGFRA) polypeptide comprising an amino acid sequence as set forth in SEQ ID NO: 27, or a fragment thereof comprising at least 10 contiguous amino acids including at least one variant amino acid site as set forth in one or more of positions 560 through 571 or 841 through 848 of SEQ ID NO: 27.
2. (currently amended) The isolated variant PDGFRA polypeptide of claim 1, comprising an amino acid sequence as set forth in SEQ ID NO: 4, 6, 8, 10, 12, 21, 23, or 25, or a fragment thereof comprising at least 10 contiguous amino acids including the variant site as set forth in one or more of position 842 of SEQ ID NO: 4, 841 and 842 of SEQ ID NO: 6, 845 and 846 of SEQ ID NO: 8, 561 and 562 of SEQ ID NO: 10, 565 and 566 of SEQ ID NO: 12, 561 of SEQ ID NO: 21, 559 and 560 of SEQ ID NO: 23, or 841 and 842 of SEQ ID NO: 25, respectively.
3. (original) The isolated variant PDGFRA polypeptide of claim 2, comprising the amino acid sequence as set forth in SEQ ID NO: 4.
4. (original) The isolated variant PDGFRA polypeptide of claim 2, comprising the amino acid sequence as set forth in SEQ ID NO: 6.
5. (original) The isolated variant PDGFRA polypeptide of claim 2, comprising the amino acid sequence as set forth in SEQ ID NO: 8.
6. (original) The isolated variant PDGFRA polypeptide of claim 2, comprising the amino acid sequence as set forth in SEQ ID NO: 10.
7. (original) The isolated variant PDGFRA polypeptide of claim 2, comprising the amino acid sequence as set forth in SEQ ID NO: 12.

8. (original) The isolated variant PDGFRA polypeptide of claim 2, comprising the amino acid sequence as set forth in SEQ ID NO: 21.

9. (original) The isolated variant PDGFRA polypeptide of claim 2, comprising the amino acid sequence as set forth in SEQ ID NO: 23.

10. (original) The isolated variant PDGFRA polypeptide of claim 2, comprising the amino acid sequence as set forth in SEQ ID NO: 25.

11. (original) An isolated nucleic acid molecule encoding the protein according to claim 1.

12. (original) An isolated nucleic acid molecule encoding the protein according to claim 2.

13. (original) The isolated nucleic acid molecule of claim 12, comprising a nucleotide sequence as set forth in SEQ ID NO: 3, 5, 7, 9, 11, 20, 22, or 24; or a fragment thereof comprising a variant nucleic acid sequence shown in one or more of position 2919 of SEQ ID NO: 3, 2917 and 2918 of SEQ ID NO: 5, 2927 and 2928 of SEQ ID NO: 7, 2075 to 2080 of SEQ ID NO: 9, 2089 to 2093 of SEQ ID NO: 11, 2076 of SEQ ID NO: 20, 2017 and 2072 of SEQ ID NO: 22, or 2916 to 2919 of SEQ ID NO: 24.

14. (original) A recombinant nucleic acid molecule comprising a promoter sequence operably linked to nucleic acid molecule according to claim 11.

15. (original) A cell transformed with a recombinant nucleic acid molecule according to claim 14.

15.16 (currently amended) A method of detecting a biological condition associated with an activating PDGFRA mutation in a subject, comprising determining whether the subject has an activating mutation in PDGFRA, and wherein the activating mutation comprises a variant

nucleic acid sequence shown in one or more of positions 2072 through 2107 or 2090 through 2937 of SEQ ID NO: 26.

16.17. (currently amended) The method of claim 1516, wherein the activating mutation comprises a variant nucleic acid sequence shown in one or more of position 2919 of SEQ ID NO: 3, 2917 and 2918 of SEQ ID NO: 5, 2927 and 2928 of SEQ ID NO: 7, 2075 to 2080 of SEQ ID NO: 9, 2089 to 2093 of SEQ ID NO: 11, 2076 of SEQ ID NO: 20, 2017 and 2072 of SEQ ID NO: 22, or 2916 to 2919 of SEQ ID NO: 24.

17.18. (currently amended) The method of claim 1516, which is a method of detecting neoplasia.

18.19. (currently amended) The method of claim 1718, wherein the neoplasia comprises a GIST.

19.20 (currently amended) The method of claim 1516, comprising:
reacting at least one PDGFRA molecule contained in a clinical sample from the subject with a reagent comprising a PDGFRA-specific binding agent to form a PDGFRA:agent complex.

20.21. (currently amended) The method of claim 1920, wherein the PDGFRA molecule is a PDGFRA encoding nucleic acid or a PDGFRA protein.

21.22. (currently amended) The method of claim 1920, wherein the PDGFRA specific binding agent is a PDGFRA oligonucleotide or a PDGFRA protein specific binding agent.

22.23. (currently amended) The method of claim 1920, wherein the sample comprises a neoplastic cell or is prepared from a neoplastic cell.

23.24. (currently amended) The method of claim 152016 wherein the PDGFRA molecule is a PDGFRA encoding nucleic acid sequence.

24.25. (currently amended) The method of claim 2324, wherein the method comprises HPLC denaturation analysis of a PDGFRA-encoding nucleic acid molecule.

25.26. (currently amended) The method of claim 2324, wherein the agent comprises a labeled nucleotide probe.

26.27. (currently amended) The method of claim 2524, wherein the nucleotide probe has a sequence selected from the group consisting of:

(a) SEQ ID NO: 3, 5, 7, 9, 11, 20, 22, or 24;
(b) fragments of (a) at least 15 nucleotides in length, and including the sequence shown in position(s) 2919 of SEQ ID NO: 3, 2917 and 2918 of SEQ ID NO: 5, 2927 and 2928 of SEQ ID NO: 7, 2075 to 2080 of SEQ ID NO: 9, 2089 to 2093 of SEQ ID NO: 11, 2076 of SEQ ID NO: 20, 2017 and 2072 of SEQ ID NO: 22, or 2916 to 2919 of SEQ ID NO: 24.

27.28. (currently amended) The method of claim 1516, further comprising *in vitro* amplifying a PDGFRA nucleic acid prior to detecting the activating PDGFRA mutation.

28.29. (currently amended) The method of claim 2728, wherein the PDGFRA nucleic acid is *in vitro* amplified using at least one oligonucleotide primer derived from a PDGFRA-protein encoding sequence.

29.30. (currently amended) The method of claim 2829, wherein at least one oligonucleotide primer comprises at least 15 contiguous nucleotides from SEQ ID NO: 3, 5, 7, 9, 11, 20, 22, or 24.

30.31. (currently amended) The method of claim 2829, wherein at least one oligonucleotide primer comprises a sequence as represented by at least 15 contiguous nucleotides shown in position(s) 2919 of SEQ ID NO: 3, 2917 and 2918 of SEQ ID NO: 5, 2927 and 2928 of SEQ ID NO: 7, 2075 to 2080 of SEQ ID NO: 9, 2089 to 2093 of SEQ ID NO: 11, 2076 of SEQ ID NO: 20, 2017 and 2072 of SEQ ID NO: 22, or 2916 to 2919 of SEQ ID NO: 24.

31.32. (currently amended) The method of claim 2021, wherein the PDGFRA molecule is a PDGFRA protein.

32.33. (currently amended) The method of claim 3132, wherein the complexes are detected by western blot assay.

33.34. (currently amended) The method of claim 3132, wherein the complexes are detected by ELISA.

34.35. (currently amended) The method of claim 3132, wherein the PDGFRA protein comprises a sequence selected from the group consisting of SEQ ID NO: 4, 6, 8, 19, 12, 21, 23, and 25.

35.36. (currently amended) The method of claim 3132, wherein the PDGFRA-specific binding agent is a PDGFRA-specific antibody or a functional fragment thereof.

36.37. (currently amended) The agent of claim 3536, wherein the agent is an antibody.

37.38. (currently amended) The antibody of claim 3637, wherein the antibody is a monoclonal antibody.

38.39. (currently amended) The monoclonal antibody of claim 3738, which monoclonal antibody recognizes an epitope of a variant PDGFRA and not an epitope of wildtype PDGFRA.

39.40. (currently amended) The monoclonal antibody of claim 3839, which recognizes an epitope of a variant PDGFRA having an amino acid sequence as shown in SEQ ID NO: 4, 6, 8, 10, 12, 21, 23, or 25.

41.42. (currently amended) The method of claim 3536, wherein the antibody is reactive to an epitope including the amino acid sequence shown in position(s) 842 of SEQ ID NO: 4, 841

and 842 of SEQ ID NO: 6, 845 and 846 of SEQ ID NO: 8, 561 and 562 of SEQ ID NO: 10, 565 and 566 of SEQ ID NO: 12, 561 of SEQ ID NO: 21, 559 and 560 of SEQ ID NO: 23, or 841 and 842 of SEQ ID NO: 25.

41.42. (currently amended) A kit for detecting an activating PDGFRA mutation in a subject using the method of claim 3432, comprising a PDGFRA protein specific binding agent.

42.43. (currently amended) The kit of claim 4142, wherein the agent is capable of specifically binding to an epitope within a PDGFRA variant protein but not to an epitope of wildtype PDGFRA.

43.44. (currently amended) The kit of claim 4243, wherein the agent is capable of specifically binding to an epitope within:

(a) the amino acid sequence shown in SEQ ID NO: 4, 6, 8, 10, 12, 21, 23, or 25;
or

(b) antigenic fragments of (a) that comprise the sequence shown in position(s) 842 of SEQ ID NO: 4, 841 and 842 of SEQ ID NO: 6, 845 and 846 of SEQ ID NO: 8, 561 and 562 of SEQ ID NO: 10, 565 and 566 of SEQ ID NO: 12, 561 of SEQ ID NO: 21, 559 and 560 of SEQ ID NO: 23, or 841 and 842 of SEQ ID NO: 25.

44.45. (currently amended) The kit of claim 4142, further comprising a means for detecting binding of the PDGFRA protein binding agent to a PDGFRA polypeptide.

4546. (currently amended) The kit of claim 4142, wherein the subject is a mammal.

46.47. (currently amended) The kit of claim 4546, wherein the mammal is a human.

47.48. (currently amended) The kit of claim 4142, wherein the PDGFRA protein binding agent is an antibody.

48.49. (currently amended) A kit for determining whether or not a subject has a biological condition associated with an activating PDGFRA mutation by detecting a mutant PDGFRA sequence in the subject, comprising:

 a container comprising at least one oligonucleotide specific for a PDGFRA mutation sequence; and

 instructions for using the kit, the instructions indicating steps for:

 performing a method to detect the presence of mutant PDGFRA nucleic acid in the sample; and

 analyzing data generated by the method,

wherein the instructions indicate that presence of the mutant nucleic acid in the sample indicates that the individual has or is predisposed to the biological condition.

49.50. (currently amended) The kit of claim 4849, wherein the method to detect the presence of mutant PDGFRA nucleic acid in the sample comprises HPLC denaturation of a PDGFRA-encoding nucleic acid molecule.

50.51. (currently amended) The kit of claim 4849, further comprising a container that comprises a detectable oligonucleotide.

51.52. (currently amended) The kit of claim 4849, wherein the biological condition associated with the activating PDGFRA mutation is neoplasia.

52.53. (currently amended) The method of claim 4849, wherein the at least one oligonucleotide specific for a PDGFRA mutation sequence comprises the sequence shown in position(s) 2919 of SEQ ID NO: 3, 2917 and 2918 of SEQ ID NO: 5, 2927 and 2928 of SEQ ID NO: 7, 2075 to 2080 of SEQ ID NO: 9, 2089 to 2093 of SEQ ID NO: 11, 2076 of SEQ ID NO: 20, 2017 and 2072 of SEQ ID NO: 22, or 2916 to 2919 of SEQ ID NO: 24.

53.54. (currently amended) The method of claim 5152, wherein the neoplasia comprises a GIST.

54. (canceled)

55. (canceled)

56. (canceled)

57-58. (currently amended) A method of screening for a compound useful in influencing PDGFRA-mediated neoplasia in a mammal, comprising determining if a test compound binds to or interacts with the polypeptide or fragment according to claim 1, and selecting a compound that so binds.

535859. (currently amended) The method of claim 5758, wherein binding of the compound inhibits a PDGFRA protein biological activity.

59-60. (currently amended) The method of claim 5758, wherein the test compound is applied to a test cell.

60-61. (currently amended) A compound selected by the method of claim 5758.

61-62. (currently amended) The compound of claim 6061, for use as a therapeutic agent.

62-63. (currently amended) A composition comprising at least one antigenic fragment of the protein of claim 1, where the antigenic fragment includes the variant sequence as shown at position(s) 842 of SEQ ID NO: 4, 841 and 842 of SEQ ID NO: 6, 845 and 846 of SEQ ID NO: 8, 561 and 562 of SEQ ID NO: 10, 565 and 566 of SEQ ID NO: 12, 561 of SEQ ID NO: 21, 559 and 560 of SEQ ID NO: 23, or 841 and 842 of SEQ ID NO: 25.